

## RESEARCH ARTICLE

# Comparing the treatment of endometriosis-related pain by excision of endometriosis or hysterectomy: A multicentre prospective cohort study

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## Abstract

**Objective:** To compare the effectiveness of endometriosis excision alone to excision plus hysterectomy, with and without bilateral oophorectomy, for endometriosis-related symptoms.

**Design:** Multicentre prospective cohort.

**Setting:** Eighty-six specialist endometriosis centres.

**Population:** Women undergoing rectovaginal endometriosis surgery between 2009 and 2021.

**Methods:** We performed multivariable regression with random effects for patient and centre, controlling for age, BMI, smoking, laparoscopic versus open approach and type of bowel surgery performed, with sensitivity analysis for loss to follow-up.

**Main Outcome Measures:** Pain scores, bowel symptoms and quality-of-life measures.

**Results:** Compared to endometriosis excision alone, women undergoing hysterectomy with conservation of ovaries had greater improvement in non-cyclical pain (MD: 1.41/10, 95% CI: 1.03–1.78,  $p < 0.001$ ), dyspareunia (MD: 1.12/10, 95% CI: 0.71–1.53,  $p < 0.001$ ), back pain (MD: 1.29/10, 95% CI: 0.92–1.67,  $p < 0.001$ ) and quality-of-life scores (MD: 8.77/100, 95% CI: 5.79–11.75,  $p < 0.001$ ) at 24 months post-operatively. Women undergoing hysterectomy with bilateral oophorectomy also had greater improvement in non-cyclical pelvic pain (MD: 2.22/10, 95% CI: 1.80–2.63,  $p < 0.001$ ), dyspareunia (MD: 1.05/10, 95% CI: 0.59–1.52,  $p < 0.001$ ), back pain (MD: 1.18/10, 95% CI: 0.77–1.59,  $p < 0.001$ ) and quality of life (MD: 12.41/100, 95% CI: 9.07–15.74,  $p < 0.001$ ) at 24 months compared to endometriosis excision alone. Compared to hysterectomy with ovarian conservation, hysterectomy with bilateral oophorectomy was associated with greater improvement in non-cyclical pelvic pain (MD: 0.81/10, 95% CI: 0.32–1.30,  $p = 0.001$ ) at 24 months and quality of life (MD: 3.74/100, 95% CI: 0.56–6.92,  $p = 0.021$ ) at 12 months, although this result was sensitive to loss to follow-up.

**Conclusions:** Patients who undergo endometriosis excision plus hysterectomy experience greater improvement in pain and quality of life compared to those who have endometriosis excision alone. There are additional benefits of bilateral oophorectomy with hysterectomy, although its value is less clear due to loss of follow-up.

## KEYWORDS

endometriosis, hysterectomy, oophorectomy, rectovaginal

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## 1 | INTRODUCTION

Endometriosis is a benign gynaecological disease characterised by endometrial-like lesions outside the uterus. It is associated with severe pelvic pain and other symptoms, which may profoundly affect quality of life. Treatment options, including hormonal therapy and surgery, aim to improve symptoms,<sup>1-3</sup> however, treatment failure is common and symptoms may persist or recur in 40%–50% of patients, requiring repeat interventions.<sup>4,5</sup>

Conservative endometriosis surgery involves excision or ablation of visible lesions, with conservation of the uterus and ovaries. An alternative treatment strategy is to perform a hysterectomy at the same time as endometriosis excision. This simultaneously induces amenorrhoea and removes adenomyosis, which commonly co-exists with endometriosis and may contribute to pelvic pain.<sup>6</sup> Where hysterectomy is performed, many patients also undergo bilateral salpingo-oophorectomy, inducing a hypo-oestrogenic state similar to that which occurs during treatment with gonadotrophin-releasing hormone agonists.

These more radical procedures carry high rates of complications, particularly in the endometriosis patient population, where surgery is known to be complex and associated with higher complication rates than for other benign conditions.<sup>7-9</sup> Surgically-induced premature menopause is also associated with a higher risk of cardiovascular disease and bone mineral density loss,<sup>10</sup> although many of these risks can be ameliorated with hormone replacement therapy.<sup>11</sup> There is also concern that damage to pelvic nerves during hysterectomy may result in postoperative bladder and bowel dysfunction.<sup>12,13</sup>

Despite the potential drawbacks of hysterectomy and bilateral oophorectomy, there is some evidence that this approach can improve the likelihood of symptom resolution, reduce recurrence and reduce further intervention compared to endometriosis excision alone.<sup>14-19</sup> However, data to support the use of hysterectomy are limited,<sup>20</sup> and no randomised trials have been conducted,<sup>21</sup> therefore further research is needed to support the use of this radical treatment option.<sup>22</sup>

The British Society for Gynaecological Endoscopy (BSGE) established the Endometriosis Centres project in 2007.<sup>23</sup> This aims to ensure that standards of clinical and surgical care are maintained through a system of accreditation with rigorous requirements including a minimum number of procedures per annum per surgeon. Endometriosis centres must prospectively submit standardised data on patients undergoing complex endometriosis surgery to a central database, including the type of surgery performed and patients' symptoms and quality-of-life before and after surgery.

The aim of this study is to compare the effectiveness of endometriosis excision alone, endometriosis excision with hysterectomy and ovarian conservation, and endometriosis excision with hysterectomy and bilateral oophorectomy for the treatment of endometriosis symptoms using the BSGE database.

## 2 | METHODS

### 2.1 | Design

We analysed routinely collected BSGE database data to compare outcomes by the type of surgical treatment.

### 2.2 | Setting

Data were collected from 86 specialist endometriosis centres with BSGE accreditation, in the United Kingdom and in other countries, including the United States, Sri Lanka, Iran, Saudi Arabia and Turkey.

### 2.3 | Population

Women who underwent surgery for deep endometriosis requiring dissection of the pararectal space at BSGE-accredited specialist centres between 2009 and 2020.

### 2.4 | Inclusion and exclusion

In order for a case to be included on the BSGE database it must be of high surgical complexity, defined as requiring dissection of the medial pararectal space or Okabayashi space. This inclusion criterion was designed by the BSGE to capture all cases of severe rectovaginal endometriosis.

Patients undergoing surgery after 31 December 2020 were excluded to allow adequate time for follow-up, as were patients with no surgical data. For the main analysis, only patients with data from a pre-operative and at least one post-operative questionnaire was included. Sensitivity analysis to determine the effect of missing outcome data was performed as previously published<sup>24</sup> using data from all patients with pre-operative symptom questionnaire data.

Patients who had previously undergone bilateral oophorectomy or hysterectomy were excluded from analysis. Patients were divided into three groups based on the type of surgery performed—endometriosis excision alone without removal of the uterus and/or all ovarian tissue, endometriosis excision with hysterectomy with conservation of one or both ovaries, and excisional endometriosis surgery with hysterectomy plus bilateral oophorectomy (bilateral salpingo-oophorectomy or removal of a single remaining ovary).

### 2.5 | Data collection

Data were collected from the patients using a questionnaire as previously described<sup>24</sup> pre-operatively, then at 6, 12 and 24 months postoperatively. The questionnaire used in this study can be found in the supplementary information. Surgical data was entered onto the database by the

performing surgical team which included intraoperative findings, procedures and complications.

## 2.6 | Main outcome measures

Groups were compared for improvement in pain, bladder and bowel symptoms and all quality of life as well as surgical complications. As hysterectomy and bilateral oophorectomy remove menstrual cycles, we only compared non-cyclical symptoms between groups. These included pain scores for non-cyclical pelvic pain, deep dyspareunia, non-cyclical dyschezia, lower back pain, bladder pain and bladder voiding difficulty, which was measured on a 0–10 numerical rating scale. Bowel function symptoms encompassing frequency, urgency, constipation and tenesmus, were assessed using 5-point Likert items according to how often the patient experienced that symptom, with the following responses: ‘never’, ‘a little of the time’, ‘some of the time’, ‘most of the time’ and ‘always’. Quality of life was assessed using the EuroQol Visual Analogue Score (EQVAS), which is a scale of 0–100 (100 representing the best and 0 representing the worst health state imaginable), as well as the EQ5D-3L questionnaire, which included 3-point Likert items for quality of life relating to pain, anxiety/depression, ability to perform usual activities, mobility and self-care.

## 2.7 | Ethical approval

The study was approved by the University College London research ethics committee (Project ID/Title: 23137/001) and the BSGE Scientific Advisory Group. All patients gave written consent for the collection of their data for research purposes. After approval from the BSGE Scientific Advisory Group, we obtained a download of all cases on the database from 2009 to 2021 inclusive.

## 2.8 | Statistical analysis

Baseline characteristics and symptom scores of patients undergoing hysterectomy and conservative surgery were compared using independent samples *t*-test and chi-squared test of proportions. *p*-values of <0.05 were considered to be statistically significant throughout.

We took a longitudinal multilevel regression modelling approach to investigate differences in improvement in symptoms and quality of life between treatment groups. For pain symptoms (0–10 scale) and EQVAS (0–100 scale), a latent interval scale was assumed and the patient responses were analysed using mixed effects linear regression fitted by restricted maximum likelihood using the ‘nlme’ R package version 3.1-162.<sup>25</sup> Bowel function symptoms (0–4 scale) and EQ5D responses (0–2 scale) were treated as ordinal and analysed using mixed-effects ordinal (proportional odds

logistic) regression fitted by Laplace's approximation using the ‘ordinal’ R package version 2022.11-16.<sup>26</sup>

All models used a random intercept for each patient, to account for within-patient correlation of repeated measures (Table S5), and each endometriosis centre, except where data were inadequate for model identification with this structure (three out of five EQ5D-3L questionnaire fields), where instead only a random intercept for patient was used. Outcomes were modelled with respect to time post-op, with a time-by-treatment interaction term providing the measure of difference in treatment effect between groups.

Multivariable model adjustment was performed for age, BMI, smoking status, surgical approach (laparoscopy vs. open) and type of bowel surgery performed. Linearity of the relationship of continuous variables to outcomes was checked-for graphically, and covariates were checked for significant interaction terms with time. Patient age, surgical approach and type of bowel surgery performed were all found to be predictors for symptom improvement, so this was controlled-for by including a time-by-covariate interaction term. Models for bowel symptoms were also adjusted for the use of opioid medication. Initially, hysterectomy with ovarian conservation and hysterectomy with bilateral oophorectomy groups were compared to the reference group of endometriosis excision alone, after which a subgroup analysis was performed by fitting the same model with hysterectomy with ovarian conservation as the reference group to allow hysterectomy with ovarian conservation and hysterectomy with bilateral oophorectomy groups to be compared. Differences in complication rates were examined by multivariable logistic regression, controlling for patient age, BMI, smoking and the type of bowel surgery performed, based on explicit ‘yes’/‘no’ responses to complication fields of the database. Patients for whom there was no complication data were excluded from the analysis of complications.

Sensitivity to loss to follow-up was tested under the ‘missing not at random’ assumption, using best/worst-case analysis as performed previously.<sup>24</sup> The models were refitted after the missing outcome data were replaced with each possible outcome in turn from best to worst (for EQVAS scores, missing data were imputed at intervals of 10 from 0 to 100), providing a range of missing outcome values over which the model term of interest remained a significant predictor of the outcome.

Statistical analysis was performed in R Studio using R version 4.2.3 for Windows (Copyright 2023 The R Foundation for Statistical Computing), using the Tidyverse, Ordinal, Nlme and Emmeans packages.

## 3 | RESULTS

### 3.1 | Patients characteristics

We included 8442 surgical cases from 86 registered BSGE endometriosis centres in the analysis. The majority of cases in the database were performed in the United Kingdom, with international centres contributing 600 (7.1%) cases

in total between them. In total, 6606 (78.2%) patients had excisional endometriosis surgery alone, 1075 (12.7%) had endometriosis excision plus hysterectomy with ovarian conservation, and 650 (7.7%) had endometriosis excision plus hysterectomy with bilateral oophorectomy. One hundred and one (1.3%) had endometriosis excision plus bilateral oophorectomy without hysterectomy and were excluded from this analysis. Patient characteristics are available in the supplementary information (Table S1, flowchart). Mean patient age was lower amongst patients who had endometriosis excision alone (33.8 years, SD 6.8) compared to the hysterectomy with ovarian conservation and hysterectomy with bilateral oophorectomy groups (41.7 years, SD 5.9 and 42.7 years, SD 5.6, respectively) (Table S1). Mean patient BMI was lower in the endometriosis excision group (25.6 kg/m<sup>2</sup>, SD 5.2) compared to the hysterectomy with ovarian conservation and hysterectomy with bilateral oophorectomy groups (27.6 kg/m<sup>2</sup>, SD 5.4 and 28.9 kg/m<sup>2</sup>, SD 6.0, respectively).

Overall follow-up rates were 85.8% at 6 months, 64.5% at 12 months and 38.5% at 24 months. Patients undergoing hysterectomy with bilateral oophorectomy had higher follow-up rates (86.5% at 6 months, 68.8% at 12 months, 45.7% at 24 months) compared to patients undergoing hysterectomy with ovarian conservation (85.3% at 6 months, 63.3% at 12 months, 35.3% at 24 months) and to patients undergoing endometriosis excision alone (85.9% at 6 months, 64.2% at 12 months, 38.1% at 24 months). Pre-operative pain and quality-of-life scores were worse amongst patients undergoing hysterectomy with bilateral oophorectomy and hysterectomy with ovarian conservation compared to those undergoing endometriosis excision alone, particularly for non-cyclical pelvic pain (mean 6.9/10 vs. 6.8/10 vs. 6.3/10, respectively), back pain (mean 7.1/10 vs. 7.2/10 vs. 6.7/10, respectively) and EQ-VAS score (mean 51.4/100 vs. 51.4/100 vs. 55.7/100, respectively) (Table S1).

### 3.2 | Pain score improvement after surgery

In the cohort as a whole, there was significant improvement at 6 months post-operatively in non-cyclical pelvic pain (2.47/10, 95% CI: 2.55–2.40,  $p < 0.001$ ), dyspareunia (2.44/10, 95% CI: 2.52–2.36,  $p < 0.001$ ), lower back pain (2.20/10,  $p < 0.001$ ), bladder pain (0.99/10, 95% CI: 1.05–0.92,  $p < 0.001$ ) and non-cyclical dyschaemia (1.36/10, 95% CI: 1.43–1.29,  $p < 0.001$ ), and this improvement was maintained at 24 months of follow-up (Table S2).

After controlling for group differences in age, BMI, smoking, surgical approach and type of bowel surgery performed; patients undergoing hysterectomy with ovarian conservation showed greater improvement in non-cyclical pelvic pain than the endometriosis excision alone group at 6 months (MD: 1.10/10, 95% CI: 0.83–1.36,  $p < 0.001$ ), 12 months (MD: 1.16/10, 95% CI: 0.86–1.45,  $p < 0.001$ ) and 24 months (MD: 1.41/10, 95% CI: 1.03–1.78,  $p < 0.001$ ). They also showed greater improvement in dyspareunia

at 6 months (MD: 0.62/10, 95% CI: 0.33–0.90,  $p < 0.001$ ), 12 months (MD: 0.82/10, 95% CI: 0.50–1.14,  $p < 0.001$ ) and 24 months (MD: 1.12/10, 95% CI: 0.71–1.53,  $p < 0.001$ ); as well as for lower back pain at 6 months (MD: 1.00/10, 95% CI: 0.73–1.26,  $p < 0.001$ ), 12 months (MD: 1.10/10, 95% CI: 0.81–1.39) and 24 months (MD: 1.29/10, 95% CI: 0.92–1.67) (Table 1 and Figure 1). Differences in symptom improvement between patients undergoing endometriosis excision alone versus hysterectomy with ovarian conservation were robust to loss to follow-up for non-cyclical pain, back pain and dyspareunia. We found no evidence of a difference in dyschaemia or bladder pain improvement between patients undergoing endometriosis excision alone and hysterectomy with ovarian conservation.

After controlling for group differences, patients undergoing hysterectomy with bilateral oophorectomy showed greater improvement from their pre-operative score for non-cyclical pelvic pain than patients undergoing endometriosis excision alone at 6 months (MD: 1.46/10, 95% CI: 1.14–1.79,  $p < 0.001$ ), 12 months (MD: 1.69/10, 95% CI: 1.33–2.04,  $p < 0.001$ ) and at 24 months (MD: 2.22/10, 95% CI: 1.80–2.63,  $p < 0.001$ ). They also demonstrated greater improvement in dyspareunia at 12 months (MD: 0.75/10, 95% CI: 0.36–1.14,  $p = 0.001$ ) and at 24 months (MD: 1.05/10, 95% CI: 0.59–1.52,  $p < 0.001$ ); as well as greater improvement in lower back pain at 6 months (MD: 0.93/10, 95% CI: 0.61–1.26,  $p < 0.001$ ), at 12 months (MD: 1.02/10, 95% CI: 0.67–1.37,  $p < 0.001$ ) and 24 months (MD: 1.18/10, 95% CI: 0.77–1.59,  $p < 0.001$ ). All of these group differences were robust to loss to follow-up. Hysterectomy with bilateral oophorectomy patients also demonstrated greater improvement in non-cyclical dyschaemia than endometriosis excision alone patients at 6 months (MD: 0.31/10, 95% CI: 0.01–0.62,  $p = 0.045$ ) and at 12 months (MD: 0.47/10, 95% CI: 0.14–0.80,  $p = 0.005$ ) and 12-months post-op, although the group difference did not remain statistically significant at 24 months post-op. There were no significant differences in bladder pain improvement between patients undergoing hysterectomy with bilateral oophorectomy versus endometriosis excision alone.

On sub-group analysis of patients undergoing hysterectomy with and without bilateral oophorectomy, patients undergoing hysterectomy with bilateral oophorectomy showed greater improvement in non-cyclical pelvic pain than hysterectomy with ovarian conservation at 12 months (MD: 0.53/10, 95% CI: 0.13–0.93,  $p = 0.010$ ) and at 24 months (MD: 0.81/10, 95% CI: 0.32–1.30,  $p = 0.001$ ). This finding was not robust to loss to follow-up if the symptom severity of those lost to follow-up was assumed to be very mild (pain score 0–1/10).

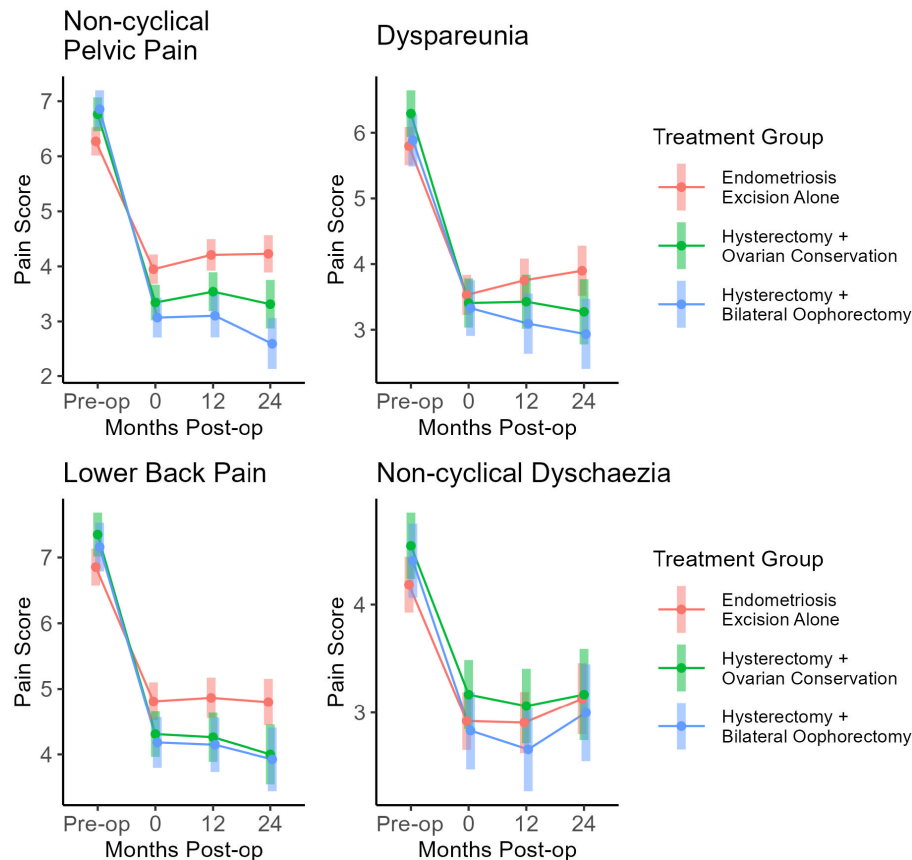
### 3.3 | Quality of life improvement after surgery

In the cohort as a whole, there was significant improvement in EQVAS scores at 6 months (MD: 16.30/100, 95% CI: 15.70–16.89,  $p < 0.001$ ), 12 months (MD: 15.31/100, 95% CI: 14.65–15.97,  $p < 0.001$ ) and 24 months (MD: 15.18/100, 95%

TABLE 1 Differences between treatment groups in symptom improvement after surgery, determined by the coefficient for the time-by-treatment interaction term in the mixed effects regression model.

Symptom	Months post-op	Hysterectomy + ovarian conservation vs. endometriosis excision alone			Hysterectomy + bilateral oophorectomy vs. endometriosis excision alone			Hysterectomy + bilateral oophorectomy vs. hysterectomy + ovarian conservation		
		Difference in symptom change from pre-op/10 (95% CI)	p Value	Robust to missing outcome data range	Difference in symptom change from pre-op/10 (95% CI)	p Value	Robust to missing outcome data range	Difference in symptom change from pre-op/10 (95% CI)	p Value	Robust to missing outcome data range
Non-cyclical pelvic pain	6	-1.10 (-1.36 to -0.83)	<0.001	0-10	-1.46 (-1.79 to -1.14)	<0.001	0-10	-0.36 (-0.73 to 0.00)	0.052	NS
	12	-1.16 (-1.45 to -0.86)	<0.001	0-10	-1.69 (-2.04 to -1.33)	<0.001	0-10	-0.53 (-0.93 to -0.13)	0.010	2-10
	24	-1.41 (-1.78 to -1.03)	<0.001	0-10	-2.22 (-2.63 to -1.80)	<0.001	0-10	-0.81 (-1.30 to -0.32)	0.001	2-10
Dyspareunia	6	-0.62 (-0.90 to -0.33)	<0.001	0-10	-0.29 (-0.65 to 0.07)	0.111	NS	0.33 (-0.08 to 0.73)	0.112	NS
	12	-0.82 (-1.14 to -0.50)	<0.001	0-10	-0.75 (-1.14 to -0.36)	0.001	0-10	0.07 (-0.37 to 0.51)	0.753	NS
	24	-1.12 (-1.53 to -0.71)	<0.001	0-10	-1.05 (-1.52 to -0.59)	<0.001	0-10	0.07 (-0.47 to 0.60)	0.812	NS
Lower back pain	6	-1.00 (-1.26 to -0.73)	<0.001	0-10	-0.93 (-1.26 to -0.61)	<0.001	0-10	0.06 (-0.30 to 0.43)	0.738	NS
	12	-1.10 (-1.39 to -0.81)	<0.001	0-10	-1.02 (-1.37 to -0.67)	<0.001	0-10	0.07 (-0.32 to 0.47)	0.712	NS
	24	-1.29 (-1.67 to -0.92)	<0.001	0-10	-1.18 (-1.59 to -0.77)	<0.001	0-10	0.11 (-0.37 to 0.60)	0.643	NS
Bladder pain	6	0.06 (-0.18 to 0.30)	0.609	NS	0.09 (-0.20 to 0.39)	0.526	NS	0.03 (-0.3 to 0.36)	0.846	NS
	12	0.12 (-0.14 to 0.39)	0.358	NS	0.16 (-0.16 to 0.48)	0.332	NS	0.03 (-0.33 to 0.39)	0.857	NS
	24	-0.29 (-0.63 to 0.04)	0.089	NS	-0.15 (-0.53 to 0.23)	0.434	NS	0.14 (-0.3 to 0.58)	0.519	NS
Non-cyclical Dyschaesia	6	-0.11 (-0.36 to 0.13)	0.367	NS	-0.31 (-0.62 to -0.01)	0.045	0-5	-0.2 (-0.54 to 0.14)	0.258	NS
	12	-0.21 (-0.48 to 0.07)	0.141	NS	-0.47 (-0.80 to -0.14)	0.005	0-10	-0.26 (-0.64 to 0.11)	0.164	NS
	24	-0.32 (-0.67 to 0.03)	0.072	NS	-0.35 (-0.74 to 0.04)	0.075	NS	-0.03 (-0.48 to 0.42)	0.893	NS

Note: All models used a random intercept for each patient and centre and were controlled for age, BMI, smoking status, surgical approach (laparoscopy/open) and type of bowel surgery performed. All pain symptoms were scored on a 0-10 numerical scale, a negative difference denotes greater symptom improvement. Results with p<0.05 are in bold.



**FIGURE 1** Modelled marginal mean pain scores over time by treatment group. Estimated marginal mean is plotted (point) with 95% confidence interval (bar).

14.37–15.98,  $p < 0.001$ ) compared to baseline, as well as in all EQ5D-QOL-3L response items (Table S2).

Compared to endometriosis excision alone, patients undergoing hysterectomy with ovarian conservation showed greater improvement in EQ-VAS score by at 6 months (MD: 8.29/100, 95% CI: 6.18–10.41,  $p < 0.001$ ), 12 months (MD: 8.23/100, 95% CI: 5.88–10.57,  $p < 0.001$ ) and 24 months (MD: 8.77/100, 95% CI: 5.79–11.75,  $p < 0.001$ ) (Table 2 and Figure 2), and these group differences were robust to missing follow-up data. Patients undergoing hysterectomy with ovarian conservation also showed greater improvement in EQ5D questionnaire response for ‘pain/discomfort’ at 6 months (aOR: of poor QOL response 0.54, 95% CI: 0.42–0.69,  $p < 0.001$ ), 12 months (aOR: 0.53, 95% CI: 0.40–0.70,  $p < 0.001$ ) and 24 months (aOR: 0.50, 95% CI: 0.35–0.70,  $p < 0.001$ ) and for ‘usual activities’ at 6 months (aOR: 0.67, 95% CI: 0.51–0.87,  $p = 0.003$ ), 12 months (aOR: 0.50, 95% CI: 0.37–0.68,  $p < 0.001$ ) and 24 months (aOR: 0.52, 95% CI: 0.35–0.77,  $p = 0.001$ ), but not for ‘anxiety/depression’, ‘self-care’ and ‘mobility’ questionnaire fields.

Compared to endometriosis excision alone, patients undergoing hysterectomy with bilateral oophorectomy showed greater improvement in EQVAS scores 6 months (MD: 10.45/100, 95% CI: 7.84–13.06,  $p < 0.001$ ), 12 months (MD: 11.97/100, 95% CI: 9.14–14.79,  $p < 0.001$ ) and 24 months (MD: 12.41/100, 95% CI: 9.07–15.74,  $p < 0.001$ ), and these

differences were robust to loss to follow-up. They also showed greater improvement in EQ5D questionnaire response for ‘pain/discomfort’ at 6 months (aOR: 0.45, 95% CI: 0.33–0.61,  $p < 0.001$ ), 12 months (aOR: 0.45, 95% CI: 0.32–0.63,  $p < 0.001$ ) and 24 months (aOR: 0.27, 95% CI: 0.18–0.40,  $p < 0.001$ ), as well as for ‘usual activities’ at 6 months (aOR: 0.47, 95% CI: 0.34–0.66,  $p < 0.001$ ), 12 months (aOR: 0.36, 95% CI: 0.25–0.53,  $p < 0.001$ ) and 24 months (aOR: 0.35, 95% CI: 0.22–0.55,  $p < 0.001$ ). Additionally, they showed greater improvement in responses for ‘mobility’ at 6 months (aOR: 0.59, 95% CI: 0.38–0.90,  $p = 0.016$ ), 12 months (aOR: 0.42, 95% CI: 0.26–0.67,  $p < 0.001$ ) and 24 months (aOR: 0.52, 95% CI: 0.30–0.91,  $p = 0.022$ ) as well as for ‘self-care’ at 12 months (aOR: 0.40, 95% CI: 0.18–0.89,  $p = 0.024$ ), but not for ‘anxiety/depression’. Other than for ‘self-care’ and ‘mobility’ at 24 months, these group differences were all robust to missing follow-up data.

On sub-group analysis, patients undergoing hysterectomy with bilateral oophorectomy showed greater improvement than those undergoing hysterectomy with ovarian conservation in EQVAS scores at 12 months (MD: 3.74/100, 95% CI: 0.56–6.92,  $p = 0.021$ ), ‘pain/discomfort’ EQ5D response at 24 months (aOR: 0.56, 95% CI: 0.35–0.89,  $p = 0.015$ ), ‘mobility’ at 12 months (aOR: 0.57, 95% CI: 0.33–0.96,  $p = 0.036$ ) and ‘self-care’ at 12 months post-operatively (aOR: 0.30, 95% CI: 0.12–0.71,  $p = 0.006$ ). Other than ‘self-care’, these were

TABLE 2 Group differences in quality of life improvement.

Months post-op	Hysterectomy + ovarian conservation vs. endometriosis excision alone			Hysterectomy + bilateral oophorectomy vs. endometriosis excision alone			Hysterectomy + bilateral oophorectomy vs. hysterectomy + ovarian conservation			
	Difference in improvement/100 (95% CI)	p Value	Robust to missing outcome data range	Difference in improvement/100 (95% CI)	p Value	Robust to missing outcome data range	Difference in improvement/100 (95% CI)	p Value	Robust to missing outcome data range	
EQVAS*	8.29 (6.18–10.41)	<0.001	0–100	10.45 (7.84–13.06)	<0.001	0–100	2.16 (–0.76–5.07)	0.147	NS	
12	8.23 (5.88–10.57)	<0.001	0–100	11.97 (9.14–14.79)	<0.001	0–100	3.74 (0.56–6.92)	0.021	0–70	
24	8.77 (5.79–11.75)	<0.001	10–100	12.41 (9.07–15.74)	<0.001	0–100	3.64 (–0.23–7.5)	0.065	NS	
EQ5D field	Months post-op	aOR poor QOL response (95% CI)	p value	Robust to missing outcome data range	aOR poor QOL response (95% CI)	p value	Robust to missing outcome data range	aOR poor QOL response (95% CI)	p value	Robust to missing outcome data range
Pain/Discomfort	6	0.54 (0.42–0.69)	<0.001	0–2	0.45 (0.33–0.61)	<0.001	0–2	0.82 (0.58–1.16)	0.257	NS
	12	0.53 (0.40–0.70)	<0.001	0–2	0.45 (0.32–0.63)	<0.001	0–2	0.83 (0.57–1.22)	0.340	NS
	24	0.50 (0.35–0.70)	<0.001	0–1	0.27 (0.18–0.40)	<0.001	0–2	0.56 (0.35–0.89)	0.015	1–2
Usual activities	6	0.67 (0.51–0.87)	0.003	0–2	0.47 (0.34–0.66)	<0.001	0–2	0.76 (0.53–1.09)	0.143	NS
	12	0.50 (0.37–0.68)	<0.001	0–2	0.36 (0.25–0.53)	<0.001	0–2	0.77 (0.52–1.15)	0.203	NS
	24	0.52 (0.35–0.77)	0.001	0–1	0.35 (0.22–0.55)	<0.001	0–2	0.76 (0.46–1.26)	0.284	NS
Anxiety depression	6	0.83 (0.63–1.09)	0.186	NS	1.01 (0.72–1.42)	0.945	NS	1.22 (0.83–1.78)	0.312	NS
	12	0.86 (0.64–1.17)	0.343	NS	1.04 (0.72–1.49)	0.848	NS	1.2 (0.79–1.81)	0.392	NS
	24	0.72 (0.48–1.07)	0.106	NS	0.76 (0.49–1.18)	0.226	NS	1.06 (0.63–1.77)	0.839	NS
Mobility	6	0.88 (0.63–1.24)	0.472	NS	0.59 (0.38–0.90)	0.016	0–2	0.66 (0.41–1.07)	0.092	NS
	12	0.74 (0.51–1.07)	0.111	NS	0.42 (0.26–0.67)	<0.001	0–2	0.57 (0.33–0.96)	0.036	1–2
	24	0.62 (0.37–1.02)	0.06	NS	0.52 (0.30–0.91)	0.022	1–2	0.84 (0.43–1.62)	0.598	NS
Self-care	6	1.57 (0.93–2.67)	0.094	NS	0.79 (0.40–1.56)	0.493	NS	0.5 (0.24–1.07)	0.074	NS
	12	1.36 (0.76–2.45)	0.304	NS	0.40 (0.18–0.89)	0.024	1–2	0.3 (0.12–0.71)	0.006	0–2
	24	1.72 (0.81–3.64)	0.158	NS	0.64 (0.26–1.55)	0.323	NS	0.37 (0.14–1.04)	0.059	NS

Note: EQ-VAS is scored on a 0–100 scale, 100 denoting the best possible quality of life and is analysed using mixed-effects linear regression as in Table 1. For EQ5D fields (0–2 scale), group differences were determined by mixed-effects ordinal regression. Models were controlled for age, BMI, smoking status, surgical approach (laparoscopy/open) and type of bowel surgery performed. All models used a random intercept for patient and centre, except for EQ5D fields 'anxiety/depression', 'mobility' and 'self-care' which used a random intercept for patient only. Results with  $p < 0.05$  are in bold.

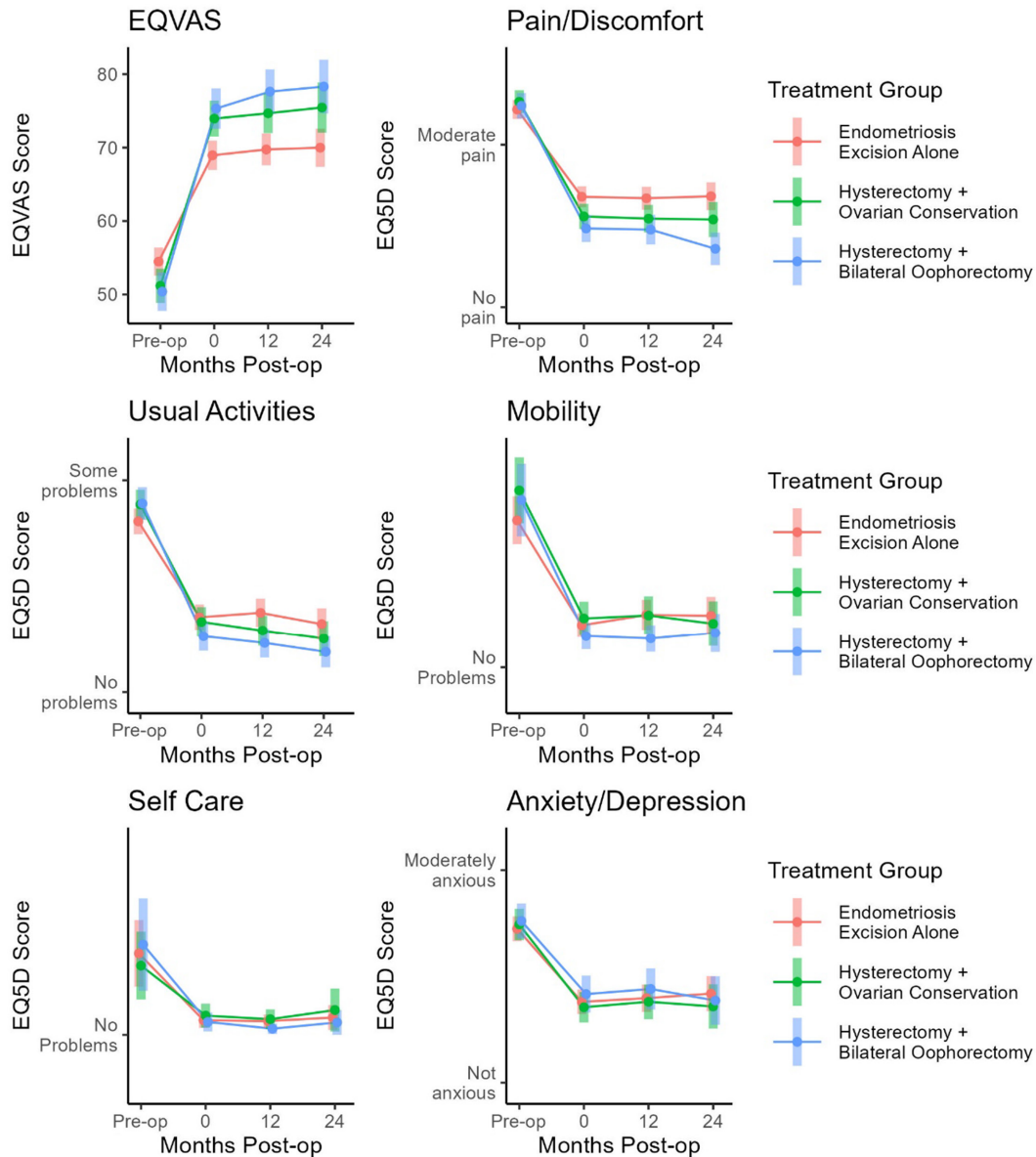


FIGURE 2 Modelled marginal mean quality of life scores over time by treatment group.

not robust to loss to follow-up if drop-out was associated with good quality of life scores.

### 3.4 | Bowel and bladder function

In the cohort overall, there was a significant improvement in all bowel and bladder function symptoms at 6 months post-operatively including diarrhoea (aOR severe symptom core: 0.78, 95% CI: 0.73–0.83,  $p < 0.001$ ), faecal urgency (aOR: 0.48, 95% CI: 0.45–0.51,  $p < 0.001$ ), tenesmus (aOR: 0.52, 95% CI: 0.48–0.55,  $p < 0.001$ ), constipation (aOR: 0.47, 95% CI: 0.44–0.50,  $p < 0.001$ ) and bladder voiding difficulty (0.43/10 improvement, 95% CI: 0.37–0.49,  $p < 0.001$ ), and these improvements remained significant over the 2-year follow-up period (Table S2). Patients undergoing hysterectomy with ovarian conservation showed significantly greater

improvement than those undergoing endometriosis excision alone in faecal urgency at 24 months follow-up (aOR: 0.68, 95% CI: 0.49–0.94,  $p = 0.020$ ) and less improvement in diarrhoea at 12 months follow-up (aOR: 1.29, 95% CI: 1.00–1.65,  $p = 0.046$ ), although this was of borderline statistical significance (Table S3). Other than these, there were no other significant differences in bowel or bladder function change between groups.

### 3.5 | Complications

Data on perioperative complications was available for 7435 (88%) patients and on late complications for 6077 (72%) of patients. In total, 319 (4.3%) suffered perioperative complications, and 201 (3.3%) suffered late complications. After adjusting for age, BMI, smoking and the type of bowel surgery

performed, patients undergoing hysterectomy with ovarian conservation had higher odds of ureteric injury (aOR: 4.84, 95% CI: 1.84–12.81,  $p=0.001$ ), conversion to laparotomy (aOR: 2.25, 95% CI: 1.04–4.76,  $p=0.036$ ) and pelvic haematoma (aOR: 6.04, 95% CI: 2.73–13.58,  $p<0.001$ ) compared to patients undergoing endometriosis excision alone (Table S4). Patients undergoing hysterectomy with bilateral oophorectomy had higher odds of haemorrhage more than 1 L (aOR: 3.36, 95% CI: 1.45–7.55,  $p=0.004$ ), ureteric injury (aOR: 5.13, 95% CI: 1.64–15.46,  $p=0.004$ ), unexpected bladder injury (aOR: 4.87, 95% CI: 1.28–19.73,  $p=0.021$ ), conversion to laparotomy (aOR: 2.38, 95% CI: 0.98–5.5,  $p=0.046$ ), pelvic haematoma (aOR: 6.18, 95% CI: 2.42–15.62,  $p<0.001$ ) and urinary tract leak (aOR: 5.78, 95% CI: 0.96–30.83,  $p=0.042$ ) compared to patients undergoing endometriosis excision alone.

## 4 | DISCUSSION

### 4.1 | Main findings

Our study provides evidence for the additional benefit of performing a total hysterectomy with endometriosis excision, compared to endometriosis excision alone, for the treatment of endometriosis-related pain and quality of life. The additional benefit of hysterectomy became more pronounced with increasing time over the 2-year follow-up period. We also find some evidence of benefit from bilateral oophorectomy in addition to hysterectomy, however, this effect is smaller and less robust to loss to follow-up. Despite the greater radicality, we find no evidence for worse post-operative bladder or bowel function after hysterectomy compared to endometriosis excision alone, however, we found a higher rate of perioperative and late complications in patients undergoing hysterectomy.

### 4.2 | Strengths and limitations

This study uses one of the largest prospective datasets globally on the surgical management of severe endometriosis. We include over 8000 cases of complex endometriosis surgery, with detailed data on surgical technique, patient symptoms and quality of life at baseline and after surgery. The multicentre nature of the study reduces the risk of bias from systematic differences in practice between centres and increases the probability that these findings represent the true additional benefit provided by hysterectomy, with and without bilateral oophorectomy.

The major limitation of this study is that it is not randomised, therefore despite controlling for multiple confounding factors, it is difficult to interpret the precise treatment effect which can be attributed to each treatment modality. Additionally, there was a considerable loss to follow-up in the study, particularly at 24 months post-operatively where there was over 50% loss in all groups. This risks the introduction of bias if the probability of loss to follow-up is correlated with a worse or better

outcome. We have tested the robustness of our findings to the extremes of this assumption, and although the majority of our findings are robust to this, some are not, particularly in the comparison between hysterectomy with ovarian conservation and hysterectomy with bilateral oophorectomy, probably due to smaller numbers in these groups.

### 4.3 | Clinical implications and future research

Our results support the current practice of performing hysterectomy in combination with endometriosis excision for selected patients in specialist centres in line with European Society of Human Reproduction and Embryology (ESHRE) guidelines.<sup>1</sup> It has previously been shown that more severe pre-operative pain is associated with worse post-operative pain scores,<sup>27–29</sup> yet despite the worse baseline symptoms in patients undergoing a hysterectomy, these patients demonstrate greater improvement in symptoms and quality of life. A randomised controlled trial would be ideal to conclusively determine the additional benefit of performing hysterectomy with or without bilateral oophorectomy, however, this is unlikely to be feasible due to recruitment and randomisation constraints, so large non-randomised cohort studies may remain the best source of data to address this question.

There are a number of ways in which hysterectomy may provide additional benefit. Inducing amenorrhoea through hysterectomy removes menstrual cramps and treats coexisting menorrhagia. Hysterectomy may provide better surgical access to allow more complete excision of pelvic lesions, reducing the risk of recurrence through incomplete excision. The removal of coexisting adenomyosis may play a major role, however it is unclear to whether this is the primary determinant of the additional pain relief conveyed by hysterectomy. In a single-centre study of 220 patients where data on adenomyosis was collected, a greater improvement in pain and quality of life was seen in those undergoing hysterectomy with bilateral oophorectomy compared to endometriosis excision alone, even after controlling for the presence of adenomyosis.<sup>16</sup> Data on the presence of adenomyosis is not routinely collected on the BSGE database, therefore it was not possible to investigate its effect on the results of this study. The diagnosis of adenomyosis can be challenging and dependent on expertise and the diagnostic modality used. Further research is needed to determine how to use the presence or absence of adenomyosis to inform patient choices prior to surgery for endometriosis.

In this study, we found moderately greater symptom and quality of life improvement in patients undergoing hysterectomy with bilateral oophorectomy compared to hysterectomy with ovarian conservation. This may be due to hypo-oestrogenism suppressing any residual endometriotic lesions, or additionally due to reduction in the symptoms of premenstrual syndrome in some patients,

for which hysterectomy with bilateral oophorectomy with add-back HRT can be effective.<sup>30</sup> A number of studies have found higher rates of symptom recurrence and repeat surgery after hysterectomy with ovarian conservation compared to hysterectomy with bilateral oophorectomy, particularly after 5 years or more of follow-up.<sup>15,31,32</sup> This must be weighed-up on an individual basis, due to risks associated with bone mineral density loss and adverse cardiovascular effects of premature menopause.<sup>33,34</sup> Hormone replacement therapy can offer prevention against osteoporotic fractures<sup>11,35</sup> and cardiovascular events.<sup>36</sup> Despite concerns over the possibility of endometriosis recurrence after HRT, this is uncommon and may be related to incomplete excision.<sup>37,38</sup> In keeping with this, recent ESHRE guidelines recommend treatment of endometriosis patients after bilateral oophorectomy with combined HRT.<sup>1</sup> It remains unclear to what extent the effect of bilateral oophorectomy can be reproduced by long-term hormonal suppression, and this is an important area for further research.

The higher rate of complications amongst patients undergoing hysterectomy in this study may be a concern for patients and is in keeping with other studies.<sup>39,40</sup> This may be partly due to more extensive disease being present or a higher number of previous conservative operations in these groups. It is important to consider the lower rate of re-operation for endometriosis seen in patients who have had a hysterectomy. When multiple endometriosis operations over a lifetime are taken into account, the possibility of suffering a complication after hysterectomy may be offset by the reduced need for repeat operations. There is also concern that the greater surgical complexity associated with hysterectomy may result in injury to pelvic nerves which orchestrate bladder and bowel function, as can occur after radical hysterectomy for cervical cancer.<sup>13,39-42</sup> In this study, we found that bladder and bowel function improved significantly over the 2-year follow-up period, and we did not find higher rates of long-term bladder or bowel dysfunction amongst patients undergoing hysterectomy with or without ovarian conservation compared to endometriosis excision alone. This is in keeping with previous studies showing that pelvic organ dysfunction due to endometriosis surgery is transitory and that overall improvement in function is likely after removal of endometriosis.<sup>43-45</sup>

Despite a thorough removal of all visible endometriosis lesions, symptoms may persist even where hysterectomy and bilateral salpingo-oophorectomy are performed. The greatest predictor of residual pain after hysterectomy for endometriosis appears to be high scores for centralised pain<sup>29</sup> stressing the importance of a detailed history and individualised and holistic care within a multidisciplinary team.

## 5 | CONCLUSION

Patients who undergo endometriosis excision plus hysterectomy experience greater improvement in endometriosis-related chronic pain and quality of life compared to those

who have endometriosis excision alone. There are additional benefits of bilateral oophorectomy, although its value is less clear due to loss of follow-up. Our findings provide the much-needed evidence to support the current clinical practice of hysterectomy for endometriosis and can be used to counsel patients undergoing surgery for severe endometriosis.

### AUTHOR CONTRIBUTIONS

JL—design of study, applying for ethical approval, data preparation, statistical analysis, clinical interpretation, writing and amending manuscript, submitting for publication. AV and ES—conception and design of study, applying for ethical approval, obtaining and analysing data, clinical interpretation, amending manuscript. MH and BHA-W—conception and design of study, obtaining and analysing data, clinical interpretation, amending manuscript.

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### CONFLICT OF INTEREST STATEMENT

None of the authors have any competing interests to disclose.

### DATA AVAILABILITY STATEMENT

The data used in this study are available from the British Society for Gynaecological Endoscopy (BSGE). Restrictions apply to the availability of these data, which were used under licence for this study. Data are available from the authors with the permission of the BSGE.

### ETHICS APPROVAL

All patients gave written consent to the collection of data from their questionnaires and surgical data from their operations to be stored in the BSGE database and used subsequently for research and publication. The data is stored in an encrypted form and hosted by a paid third party. We obtained approval from the BSGE Scientific Advisory Group for research use of the database, who then provided the data in anonymised form. We also obtained approval from the University College London Research Ethics Committee to undertake this study (Project ID/Title: 23137/001: Which patient factors are predictive for symptoms, outcomes and type of surgery performed for severe endometriosis? A national database study).

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## SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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